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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/590,026	08/18/2006	Nobuhiro Oikawa	OIKAWAI	5830
1444	7590	03/04/2011	EXAMINER	
Browdy and Neimark, PLLC			RICCI, CRAIG D	
1625 K Street, N.W.				
Suite 1100			ART UNIT	PAPER NUMBER
Washington, DC 20006			1628	
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		03/04/2011	PAPER	

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/590,026	<b>Applicant(s)</b> OIKAWA ET AL.
	<b>Examiner</b> CRAIG RICCI	<b>Art Unit</b> 1628

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on **28 December 2010**.  
 2a) This action is **FINAL**.      2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) **1,2,6,7,9 and 14-17** is/are pending in the application.  
 4a) Of the above claim(s) **15-17** is/are withdrawn from consideration.  
 5) Claim(s) \_\_\_\_\_ is/are allowed.  
 6) Claim(s) **1-2, 6-7 and 9** is/are rejected.  
 7) Claim(s) \_\_\_\_\_ is/are objected to.  
 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

1) Notice of References Cited (PTO-892)  
 2) Notice of Draftsperson's Patent Drawing Review (PTO-442)  
 3) Information Disclosure Statement(s) (PTO-SB/08)  
 Paper No(s)/Mail Date \_\_\_\_\_

4) Interview Summary (PTO-413)  
 Paper No(s)/Mail Date \_\_\_\_\_

5) Notice of Informal Patent Application  
 6) Other: \_\_\_\_\_

**DETAILED ACTION**

**Status of the Claims**

1. The amendments filed 12/28/2010 were entered.

**Response to Arguments**

2. Applicant's arguments, filed 12/28/2010, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. In particular, the rejection of claims under 35 U.S.C. 112, first paragraph, has been withdrawn in view of Applicant's arguments. Although it is noted than many of the compounds relied upon by Applicant as evidence of enablement are not within the claimed genus, it is considered persuasive that the demonstrated activity of said compounds, along with the compounds that are within the genus of Formula (1), is sufficient to establish enablement of the compounds as claimed. As such, Applicant's arguments directed to the withdrawn rejection is rendered moot. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

**Election/Restrictions**

3. Newly submitted claims 15-17 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: the claims are directed to a method of using the elected invention and, as previously discussed, lack the same or corresponding special technical feature with the elected invention. Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly,

claims 15-17 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

#### **Claim Objections**

4. Claim 1 is objected to because of the following informalities: claim 1 recites that "R2 selected from". It would be more clear to recite "R2 is selected from"

#### **Claim Rejections - 35 USC § 103**

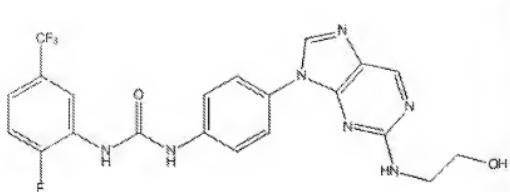
5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

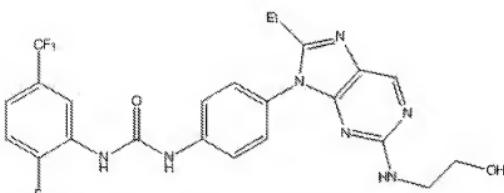
7. **Claims 1-2, 6-7, 9 and new claim 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Adams et al (WO 2003/029209).**

8. Instant claim 1 is drawn to a compound of formula 1 which encompasses the following compound species



(Species 1) wherein, in

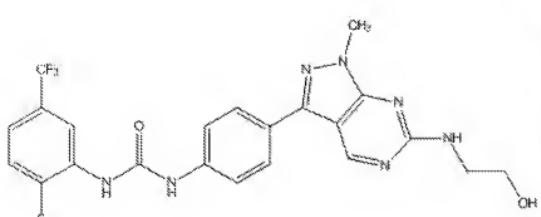
formula 1, R<sup>1</sup> is H; R<sup>2</sup> is a C<sub>1</sub> alkyl substituted with halogen atoms; R<sup>3</sup> and R<sup>4</sup> are H; R<sup>5</sup> is a halogen atom; Z<sup>1</sup> and Z<sup>2</sup> are H; R<sup>6</sup> and R<sup>7</sup> are H; Q is Formula 2 wherein Y<sup>1</sup> is hydrogen and W is -NRaRb wherein Ra is H and Rb is a C<sub>2</sub> alkenyl group substituted with Y<sup>3</sup> wherein Y<sup>3</sup> is -ORz and Rz is H; and



(Species 2) wherein, in

formula 1, R<sup>1</sup> is H; R<sup>2</sup> is a C<sub>1</sub> alkyl substituted with halogen atoms; R<sup>3</sup> and R<sup>4</sup> are H; R<sup>5</sup> is a halogen atom; Z<sup>1</sup> and Z<sup>2</sup> are H; R<sup>6</sup> and R<sup>7</sup> are H; Q is Formula 2 wherein Y<sup>1</sup> is C<sub>2</sub> alkenyl and W is -NRaRb wherein Ra is H and Rb is a C<sub>2</sub> alkenyl group substituted with Y<sup>3</sup> wherein Y<sup>3</sup> is -ORz and Rz is H

9. As discussed in the previous Action mailed 8/30/2010, and reiterated largely as follows, Adams et al teach the following compound species



which is disclosed as an inhibitor of TIE-2 kinase, VEGFR-2 kinase, and VEGFR-3 kinase.

10. The compound disclosed by Adams et al differs from the instantly claimed compounds species in two ways: (1) the arrangement of nitrogen atoms within Q; and (2) the substitution of Q with Y wherein Y is a methyl group as compared to no substitution or substitution with an ethyl group.

11. As stated by MPEP 2144.09:

A *prima facie* case of obviousness may be made when chemical compounds have very close structural similarities and similar utilities. "An obviousness rejection based on similarity in chemical structure and function entails the motivation of one skilled in the art to make a claimed compound, in the expectation that compounds similar in structure will have similar properties." *In re Payne*, 606 F.2d 303, 313, 203 USPQ 245, 254 (CCPA 1979).

. Furthermore:

Compounds which are position isomers (compounds having the same radicals in physically different positions on the same nucleus) or homologs (compounds differing regularly by the successive addition of the same chemical group, e.g., by -CH<sub>2</sub>- groups) are generally of sufficiently close structural similarity that there is a presumed expectation that such compounds possess similar properties. *In re Wilder*, 563 F.2d 457, 195 USPQ 426 (CCPA 1977).

12. In the instant case, the prior art compound taught by Adams et al is structurally similar to the instantly claimed compounds. Furthermore, any subtle differences that may stem from the shift of nitrogen atoms within the ring taught by Adams et al or the addition or subtraction of a the same chemical group (i.e., -CH<sub>2</sub>) to arrive at the instantly claimed are irrelevant since the MPEP 2144.09 states "[c]ompounds which are position isomers (compounds having the same radicals in physically different positions on the same nucleus) or homologs (compounds differing regularly by the successive addition of the same chemical group, e.g., by -CH<sub>2</sub>- groups) are generally of sufficiently close structural similarity that there is a presumed expectation that such compounds possess similar properties. *In re Wilder*, 563 F.2d 457, 195 USPQ 426 (CCPA 1977).

13. Thus, in view of *In re Payne* and *In re Wilder*, a prima facie case of obviousness exists between the claimed compound species and the structurally similar prior art compound species expected as having similar properties.

14. As such, instant claims 1-2, 6-7 and new claim 14 are rejected as prima facie obvious.

15. Instant claim 9 is drawn to a pharmaceutical composition comprising the compound of claim 1 as an active ingredient. Adams et al specifically teach “compositions and medicaments” (Page 1, Line 6) of the compound species which encompasses a pharmaceutical composition comprising the compound as an active ingredient. As such, instant claim 9 is also rejected as prima facie obvious.

16. Applicant traverses on the grounds that the instantly claimed compounds “have been demonstrated to inhibit Raf kinase” whereas “Adams does not disclose or suggest any effect on Raf inhibitory activity” (Applicant Arguments, Page 15). As such, Applicant contends that “[s]ince there is no indication that the Adams compounds have any effect on Raf kinase activity, there would be no reason for one skilled in the art to modify the Adams compounds with any reasonable expectation that the modified compounds would have Raf-kinase-inhibiting activity” (Applicant Arguments, Page 16). However, the skilled artisan would have been motivated to modify the compound taught by Adams et al to provide structurally related compounds which inhibit TIE-2 kinase, VEGFR-2 kinase, and VEGFR-3 kinase, with a reasonable expectation of success. The fact that the skilled artisan would not have predicted the modified compounds to function as Raf-kinase inhibitors is irrelevant since the instant claims are directed to compounds, not methods of their use to inhibit Raf-kinase. As such, Applicant’s argument is not found persuasive and the rejection of claims is maintained. **However**, Applicant is advised that the

showing of Raf-kinase-inhibiting activity by the instant compounds might be considered an unexpected result sufficient to overcome a rejection based on 35 U.S.C. 103(a) if factual evidence comparing the claimed invention with that of the compounds of Adams et al demonstrates that (A) the compounds of Adams et al lack Raf-kinase-inhibiting activity; and/or (B) the instant compounds exhibit superior Raf-kinase-inhibiting activity. Since no such comparison has been introduced, unexpected results have not been established.

17. Thus, for all the foregoing reasons, instant claims 1-2, 6-7, 9 and new claim 14 are rejected as *prima facie* obvious.

#### **Conclusion**

No new ground(s) of rejection are presented in this Office action except that the previous rejection is now applied to new claim 14 based on the same grounds. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CRAIG RICCI whose telephone number is (571) 270-5864. The examiner can normally be reached on Monday through Thursday, and every other Friday, 7:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Padmanabhan "Paddy" Sreenivasan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/CRAIG RICCI/  
Examiner, Art Unit 1628